REMARKS

Claims 7-9 are pending in the present Application. Claims 1-6 and 9-10 have been cancelled, claims 7 and 8 have been amended, and claim 11 have been added, leaving Claims 7-8 and 11 for consideration upon entry of the present Amendment.

The Specification has been amended to correct certain formatting errors, as explained in detail below. The specification has also been amended to cross-reference related applications.

Claims 7 and 8 have been amended to better define the invention. Support for these amendments can be found at least at page 4, lines 4-5, 23-24; page 8, lines 14-18; page 10, lines 8-35; Tables 1 and 2, and throughout the specification.

Claim 11 has been added to further claim the invention. Antecedent basis for claim 11 is found at least at Tables 1 and 2, and throughout the specification.

No new matter has been introduced by these amendments. Reconsideration and allowance of the claims are respectfully requested in view of the above amendments and the following remarks.

Examiner Interview

Applicants thank Examiner Jeanine Goldberg for the courtesy of a brief telephonic interview with Applicant's representative (Ian Lodovice) on June 10, 2008. During the interview, the § 112, first paragraph, and § 112, second paragraph, rejections were discussed.

Specification

The specification has been amended to correct certain formatting errors regarding the use of trademarks noted in the Office Action. Specifically, the specification has been amended to capitalize the trademarked company name, SEQUENOM. Further, Applicants have identified the term MassEXTEND™ as a trademark. Applicants note that "MassEXTEND™" is the correct representation of this trademark since the trademark is used as "MassEXTEND™".

The disclosure was objected to because the specification contains an embedded hyperlink. (Office Action dated 3/13/2008, page 4) The specification has been amended to

delete the embedded hyperlink and/or other form of browser-executable code.

No new matter has been introduced by these amendments. Applicants respectfully request a withdrawal of this objection.

Priority

In the Office Action, the Examiner acknowledged the Applicants claim for foreign priority based on application filed in Korea on February 2, 2004 (Korean Application No. 10-2004-0011327) and February 18, 2005 (Korean Application No. 10-2005-0013395). (Office Action dated 3/13/2008, page 3) However, the Examiner noted that certified copies of each of the foreign applications have not been filed. (Office Action dated 3/13/2008, page 3) Further, the Examiner stated that it is unclear whether the foreign document filed on 9/16/2005 is a certified copy of one of the foreign priority documents. (Office Action dated 3/13/2008, page 3)

The pending application is a 371 national stage of PCT/KR05/00465, which claimed priority to Korean Application No. 10-2004-0011327 and Korean Application No. 10-2005-001339. Applicants note that the Korean language document filed 9/16/2005 noted by the Examiner is a copy of the original Korean language PCT application. Applicants note that certified copies of the priority documents were provided to WIPO in the International phase of the application and should have been sent to the US PTO by WIPO. Applicants direct the Examiners attention the "NOTICE OF ACCEPTANCE OF APPLICATION UNDER 35 U.S.C. 371 AND 37 CFR 1.495" (FORM PCT/DO/EO/903), dated March 9, 2007, which indicates that the Priority Documents were filed on 09/16/2005.

The specification has been amended herein to include the section CROSS-REFERENCE TO RELATED APPLICATIONS, including the relationship of the related applications.

Claim Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 7-9 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. (Office Action dated 3/13/2008, page 3) In making the rejection, the

Examiner stated (a) Claim 7 is vague and indefinite because the limitation in the preamble (diagnosis of colorectal cancer) is not recited in the process steps and it is unclear whether diagnosis is accomplished by practicing the recited method steps; (b) Claim 7 is vague and indefinite because it is unclear if the parenthetical recitation (position 101) is meant to be a limitation; and (c) Claim 9 is vague and indefinite because the term "higher likelihood" is a relative term. (Office Action dated 3/13/2008, pages 3-4)

As amended, claim 7 is generally directed to a method of determining risk of developing colorectal cancer, which recites the process steps of determining in a nucleic acid sample from a Korean human the nucleotide base at a polymorphic site at position 101 of SEQ ID NO: 5, and determining risk of developing colorectal cancer in the human, wherein determining the base is guanine (G) indicates an increased risk of developing colorectal cancer compared to determining the base is thymine (T). Applicants believe that claims 7 and 8, as amended, meet the requirements of 35 U.S.C. § 112, second paragraph. .

Applicants respectfully request a withdrawal of the rejection of claims 7 and 8 under 35 U.S.C. § 112, second paragraph, and an allowance of the claims.

Claim Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 7-9 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement because the claims contain subject matter that was not described in the specification in such a way as to reasonably convey to a person skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed. (Office Action dated 3/13/2008, page 4) Applicants respectfully traverse this rejection.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. *See, e.g., Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319 (Fed. Cir. 2003); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563, (Fed. Cir. 1991).

In making the rejection, the Examiner stated that the claims are broadly drawn to a method of diagnosing colorectal cancer in any individual. Since the term "individual" is not

defined, the Examiner interpreted this term to encompass any organism. (Office Action dated 3/13/2008, page 4) Applicants note that independent claim 7 has been amended to recite "A method of determining risk of developing colorectal cancer in a Korean human".

The Office Action also stated the method of claim 8 broadly reads on immobilizing any sequence comprising any 10 or more contiguous nucleotides of SEQ ID NO:5 along with any 11^{th} nucleotide to an array and therefore does not require that the polymorphic site be within 10 or more contiguous nucleotides. (Office Action dated 3/13/2008, pages 5-7) Applicants respectfully disagree with this interpretation of claim 8. However, to facilitate prosecution, claim 8 is amended to clarify the structure of the polynucleotide immobilized on the microarray. Specifically, amended claim 8 recites "hybridizing the nucleic acid sample onto a microarray on which is immobilized a polynucleotide comprising (a) at least 10 contiguous nucleotides of SEQ ID NO: 5 comprising position 101, or (b) the complement of (a); and detecting a hybridization result."

The Office Action further stated regarding the method of claims 7 and 9, that they do not recite any steps for determining the nucleotide of polymorphic site at position 101 within polynucleotide of SEQ ID NO:5. The Office Action then stated that the claims therefore broadly encompass examining "sequences in linkage disequilibrium (LD)" with the polymorphic site (position 101) within polynucleotide of SEQ ID NO:5 and that a representative number of species of SNPs in LD with the polymorphic site at position 101 of SEQ ID NO:5 has not been presented. (Office Action dated 3/13/2008, pp 5-9, e.g., page 5, lines 1-4 and 9-16) Applicants are somewhat confused regarding this particular written description issue being alleged by the Examiner with regard to claim 7.

As amended, claim 7 is directed to a method of determining risk of developing colorectal cancer comprising determining in a nucleic acid sample from a Korean human the nucleotide base at a polymorphic site at position 101 of SEQ ID NO: 5, and determining risk of developing colorectal cancer in the human, wherein determining the base is guanine (G) indicates an increased risk of developing colorectal cancer compared to determining the base is thymine (T).

Applicants note that claim 7 recites "determining … the nucleotide base at a polymorphic site at position 101 of SEQ ID NO: 5". Claim 7 does NOT recite, as seemingly

alleged in the Office Action, determining the sequence of a member of some unspecified genus of sequences, nor does claim 7 recite an element of "linkage disequilibrium". With respect to the actual claim language, as clearly indicated in the Office Action on p. 5, lines 11-12, the particular SNP at position 101 of SEQ ID NO: 5 actually recited in the claim as the SNP for which the nucleotide base is determined in the method meets the written description requirement.

Applicants note that there were many conventional and well-known methods for determining the allele present at such a known SNP that were known to those of ordinary skill in the art at the time the application was filed. Information which is well known in the art need not be described in detail in the specification. See, e.g., *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379-80, 231 USPQ 81, 90 (Fed. Cir. 1986). The specification discloses at least two such methods, but many others exist. It is within the skill of the ordinary artisan in this field to select an appropriate assay method to do the determining.

Further, Applicants respectfully assert that claims 7-8 and 11 meet the written description requirement as the specification provides sufficient detail that one of ordinary skill in the art would reasonably conclude that the inventor had possession of the claimed invention. Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. See, e.g., Pfaff v. Wells Elecs., Inc., 525 U.S. 55, 68 (1998). The specification provides an actual reduction of practice of the claimed invention using one method of determining the alleles at a SNP in a population of colorectal cancer patients and in a control "normal" population in the examples and providing the results of the statistical analysis of the results in Table 1 and therefore demonstrates that the inventors possessed the claimed invention.

Therefore, in summary, Applicants believe that claims 7 and 8, as amended, meet the requirements of 35 U.S.C. § 112, first paragraph.

Applicants respectfully request a withdrawal of the rejection of claims 7 and 8 under 35 U.S.C. § 112, first paragraph, and an allowance of the claims.

Claims 7-9 stand rejected under 35 U.S.C. § 112, first paragraph, stating that the specification does not enable a person skilled in the art to make or use the invention commensurate in scope with the pending claims. (Office Action dated 3/13/2008, page 10) In making the rejection, the Examiner stated

> while being enabling for a method of diagnosing colorectal cancer in a Korean human individual, which comprises: isolating a nucleic acid sample from a Korean human individual, amplifying the sequence of SEQ ID NO: 5 by PCR, hybridizing primers to the amplified DNA, adding polymerization solution that contains a sequence terminating ddTTP and allowing an extension reaction to proceed, determining the sequence of the products by mass spectrometry in order to determine if the sequence contains a G as the polymorphic site of position 101 in SEQ ID NO:5, wherein a G is present it is determined that the patient has or will develop colorectal cancer …

(Office Action dated 3/13/2008, page 10) Applicants respectfully traverse this rejection.

"To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.' " *Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1365 (Fed. Cir. 1997). The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt*, 537 F.2d 498, 504, 190 U.S.P.Q. 214, 219 (CCPA 1976).

As noted above, claim 7 has been amended to recite "determining risk of developing colorectal cancer in a Korean human". Further, the active step of determining risk of developing colorectal cancer in the human subject by determining if the predictive allele is found is included in independent claim 7.

Further, in making the rejection, the Examiner alleged that the specification merely enables a method of determining risk of developing colorectal cancer in a Korean human comprising ": isolating a nucleic acid sample from a Korean human individual, amplifying the sequence of SEQ ID NO: 5 by PCR, hybridizing primers to the amplified DNA, adding polymerization solution that contains a sequence terminating ddTTP and allowing an extension reaction to proceed, determining the sequence of the products by mass spectrometry in order to determine if the sequence contains a G as the polymorphic site of position 101 in SEQ ID

NO:5". Applicants respectfully assert that claims 7-8 and 11 are not so limited.

Independent claim 7 requires "determining in a nucleic acid sample from a Korean human the nucleotide base at a polymorphic site at position 101 of SEQ ID NO: 5" while dependent claim 8 limits the operation of determining the nucleotide base of the polymorphic site comprises: hybridizing the nucleic acid sample onto a microarray on which is immobilized a polynucleotide comprising (a) at least 10 contiguous nucleotides of SEQ ID NO: 5 comprising position 101, or (b) the complement of (a); and detecting a hybridization result.

Applicants note there are many methods for determining the allele present at a known SNP well known to those of ordinary skill in the art. As noted in the Office Action, at least two methods were specifically disclosed in the specification: hybridizing the nucleic acid sample onto a microarray on which is immobilized a polynucleotide comprising (a) at least 10 contiguous nucleotides of SEQ ID NO: 5 comprising position 101, or (b) the complement of (a); and detecting a hybridization result (i.e., claim 8) or determining the sequence of amplified products using mass spectrometry. Applicants assert that one of ordinary skill in the art is capable of determining in a nucleic acid sample from a Korean human the nucleotide base at a polymorphic site at position 101 of SEQ ID NO: 5 without undue experimentation by any of a variety of methods, which may include the two methods specifically disclosed. However due to issues of cost, equipment availability, or skill, the artisan might choose one of the available alternative methods of performing the determination. The method selection and performance of the "determining in a nucleic acid sample from a Korean human the nucleotide base at a polymorphic site at position 101 of SEQ ID NO: 5" by the artisan of ordinary skill would not entail undue experimentation.

In summary, Applicants believe that claims 7-8 and 11 meet the enablement requirement set forth in 35 U.S.C. § 112, first paragraph.

Applicants respectfully request a withdrawal of the rejection of claims 7 and 8 under 35 U.S.C. § 112, first paragraph, and an allowance of the claims.

Claim Rejections Under 35 U.S.C. § 102(e) and 35 U.S.C. § 103(a)

Claim 7 stands rejected under 35 U.S.C. § 102(e), as allegedly anticipated by Wang

(US 2005/0228172) (hereinafter "Wang"). (Office Action dated 3/13/2008, page 18) Applicants respectfully traverse this rejection.

To anticipate a claim, a reference must disclose each and every element of the claim. *Lewmar Marine v. Varient Inc.*, 3 U.S.P.Q.2d 1766 (Fed. Cir. 1987).

Claim 8 stands rejected under 35 U.S.C. § 103(a), as allegedly unpatentable over Wang. (Office Action dated 3/13/2008, page 20) Applicants respectfully traverse this rejection.

For an obviousness rejection to be proper, the Examiner must meet the burden of establishing that all elements of the invention are disclosed in the prior art; that the prior art relied upon, or knowledge generally available in the art at the time of the invention, must provide some suggestion or incentive that would have motivated the skilled artisan to modify a reference or combined references; and that the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was make. *In re Fine*, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988). The obviousness inquiry also requires consideration of common knowledge and common sense. *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1742-43 (2007); *DyStar Textilfarben GmbH & Co. Deutschland KG v. C.H. Patrick Co.*, 464 F.3d 1356, 1367 (Fed. Cir. 2006) ("Our suggestion test is in actuality quite flexible and not only permits, but requires, consideration of common knowledge and common sense.")

Wang is generally directed to compositions and methods for identification of a large number of SNP's throughout the entire human genome. (Abstract) As noted by the Examiner, Wang (SEQ ID NO: 209468) discloses SEQ ID NO:5. However, Wang does not disclose the correlation with colorectal cancer. Therefore, Applicants respectfully assert that Wang does not teach all elements of the claimed invention, since Wang does not teach an active step of determining the base is guanine (G) indicates an increased risk of developing colorectal cancer compared to determining the base is thymine (T), as required by claims 7 and 8. Therefore, Applicants respectfully assert that claims 7-8 are not anticipated, or obvious, over Wang.

Since Wang does not teach all elements of the claimed invention, Applicants believe that claims 7-8 and 11 are not anticipated, or obvious, over Wang. Applicants respectfully request a withdrawal of the rejection of claim 7-8 under 102(e)/§ 103(a) and an allowance of

the claims.

Double Patenting

Claims 7-9 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 7-10 of copending Application No. 11451665. Applicants respectfully request that the examiner withdraw the provisional obviousness-type double patenting rejection until the claims are in final form and condition for allowance; until such time, there is no double patenting and no way to determine double patenting. MPEP § 804.01.I(B)(1).

It is believed that the foregoing amendments and remarks fully comply with the Office Action and that the claims herein should now be allowable to Applicants. Accordingly, reconsideration and allowance are requested.

If there are any additional charges with respect to this Amendment or otherwise, please charge them to Deposit Account No. 06-1130.

Respectfully submitted,

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